Supplemental Information

Background

- Most people who abuse prescription opioids **get them for free from a friend or relative**
- While age-adjusted rate for drug poisoning deaths involving **prescription opioids** has leveled in recent years, the **rate for deaths involving illicit opioids (heroin) has almost tripled since 2010**

**Opioid Overdose—Clinical Considerations**

- Acute condition, typically occurs over 1-3 hours and may be caused by:
  - Excess intake of opioids
  - Combination of opioid + CNS depressant
  - Expected respiratory effects of opioids in someone with compromised respiratory system or metabolic condition
- Opioid receptors found in the brain, including the respiratory center in the medulla
  - Opioids repress the urge to **breathe** and decrease the body’s/brain’s response to carbon dioxide, leading to respiratory depression and death
- Leads to:
  - Reduced sensitivity to changes in oxygen and carbon dioxide outside of normal ranges
  - Changes in tidal volume and respiratory frequency
  - Opioids can cause death by acute respiratory failure, hypoventilation, ↑ carbon dioxide, ↓ oxygen

**Risk Factors for Opioid Overdose and Indications for Naloxone**

- Risk factors for **unintentional opioid overdose**
  - Change in tolerance (switching between opioids, etc)
  - Mixing opioids with other CNS depressants (alcohol, benzodiazepines, etc)
  - Illness
  - Extreme dose of opioid
  - Using opioids alone, by oneself
- Risk factors for **prescription drug abuse/overdose**
  - Obtaining overlapping prescriptions from multiple providers and pharmacies
  - Taking high daily dosages of prescription pain medications
  - Having mental illness or a history of alcohol or other substance abuse
  - Living in rural areas, having low income
- Risk factors for opioid overdose and **potential indications for naloxone**
  - Opioid prescription plus:
    - Concurrent benzodiazepine prescription
    - History of smoking
    - Respiratory illness or obstruction
- Renal dysfunction or hepatic disease
- Known/suspected concurrent alcohol abuse
- Concurrent SSRI or tricyclic antidepressant prescription

**Tips for identifying patients at risk for opioid overdose**
- Pharmacy records show opioid prescription plus:
  - **Concurrent benzodiazepine prescription**
  - Nicotine replacement therapy (NRT), varenicline (*Chantix*), bupropion
  - Inhalers, corticosteroids
  - Respiratory antibiotics
  - Dialysis medications
  - Cirrhosis medications
  - Naltrexone, disulfiram
  - Concurrent SSRI or tricyclic antidepressant prescription

- Pharmacist interactions
  - Syringe purchase
  - Medication lock box purchase
  - Questions about medication disposal

**Naloxone: Background and Pharmacology**

- Naloxone (*Narcan*) is an **antidote** for **opioid** overdose only
  - Opioid receptor antagonist at mu, kappa, and delta receptors
- Works at opioid receptor to displace opioid agonists for a short time (has stronger affinity for opioid receptors than most other opioids) and reverses **clinical** and **toxic effects** of opioid overdose
- Shows little to no agonist activity
- Shows no pharmacological effect or harm in people who have not received opioids
- Takes effect in **about 3 minutes**
  - If person is not responding in this time a second dose may be administered
- Wears off in **about 30 to 90 minutes**
  - People can go back into overdose if long-acting opioids were taken (fentanyl, methadone, extended-release morphine, extended-release oxycodone)
  - People should avoid taking more opioids after naloxone administration so they don’t go back into overdose after naloxone wears off
  - People may want to take more opioids during this time because they may feel withdrawal symptoms
- What forms of naloxone are available and how should they be dispensed?
  - Intramuscular (IM)
    - 0.4 mg/mL solution for injection in 1 mL and 10 mL vials
      - Dispense 2 – 4 x 1 mL single-dose vials or 1 x 10 mL multi-dose vial
      - Dispense 2 – 4 retractable syringes, 1 – 1 ½ inch, 21 – 25 gauge, 1 – 3 mL
      - Cost ~$50 for 2 doses
    - 0.4 mg/mL auto-injector (*Evzio*)
      - 2-pack plus 1 trainer
      - Cost ~$575/pack
Intranasal (IN)
- 2 mg/2 mL prefilled syringes used with a mucosal atomization device (MAD)
  - Dispense 2 – 4 x 2 mg/2 mL Luer-Lock prefilled needleless syringes
  - Dispense 2 – 4 mucosal atomization devices (MAD 300)
    - Fits into Luer-Lock prefilled syringe
  - Cost ~$90 for 2 doses
- Nasal adapter allows for needleless delivery; no concern about needlesticks or proper needle disposal
- Naloxone absorbed directly into bloodstream through absorption in nasal epithelium
- Intranasal naloxone is not FDA approved, but several new intranasal kits are in development
- Naloxone may precipitate opioid withdrawal
  - Can be described as a severe case of influenza
  - During withdrawal there is a rebound release of norepinephrine leading to:
    - Agitation, tachycardia, tremor, anxiety, hypertension, etc.
  - Not life threatening unless there is a concurrent life-threatening condition

Education Points for Those Receiving Naloxone

- Key points ➔ use the “teach back” method and demonstration kits to provide training on overdose prevention, identification, and response
  - Purpose for naloxone
  - Correct naloxone administration
  - Precautions regarding interacting medications
  - Identifying and avoiding high-risk situations for overdose
  - Risk reduction strategies
  - Opioid overdose response

Overdose Identification and Response: Counseling Points

1. Identify overdose
2. Call 911
3. Give rescue breaths
4. Give naloxone
5. Stay until help arrives

Identify an opioid overdose

- Signs of an overdose
  - Respiratory depression (slow/shallow/no breathing)
  - Gasping for breath, gurgling/heavy wheezing or snoring sound
  - No response to stimulus
  - Blue, pale, or grayish lips/skin/fingernails
  - Low blood pressure
  - Slow heart rate
  - Pinpoint pupils
- If person is not breathing or struggling to breathe:
  - Call out their name
 Rub knuckles of a closed fist over the sternum
 If no response, they may be experiencing an overdose
  o Use instinct, if something doesn’t look right, call 911
  o Make sure person understands that if they have to leave at any time (to call 911, get naloxone ready, etc) to put patient in the rescue position
    ▪ Put them on their side with their top leg and arm crossed over their body
    ▪ This makes it difficult for them to roll over and lessens the chance that they will choke on vomit

• Call 911
  o It’s important to get emergency help ASAP
  o Reassure patients that medical help is crucial to saving lives
    ▪ Calling 911 is estimated to occur only 10-56% of the time
  o Reinforce that after identifying an overdose, call 911 immediately
    ▪ Do not wait until after administering naloxone
  o When calling 911 all that needs to be said is:
    ▪ “Someone is unresponsive and not breathing (or struggling to breathe)”
    ▪ Clear address and location
  o Be aware of reasons why people may be scared to call 911 in case of an overdose
    ▪ Police are normally notified of a 911 call involving an overdose and often come to the scene
    ▪ People may be hesitant to call if they are on parole, have outstanding arrest warrants, etc.
    ▪ Lack of Good Samaritan Law (limited immunity for drug-related charges if seek help in suspected overdose emergency)
    ▪ Lack of education on overdose or denial overdose is occurring
    ▪ Home remedies are used instead (ice bath, caffeine, etc)

• Give rescue breaths
  o During an overdose, respiratory depression occurs, and lack of oxygen is the major concern
    ▪ Giving oxygen can save a life in an overdose
  o All people receiving naloxone should be educated on how to administer rescue breathing
    ▪ Make sure people don’t think they can skip the step
  o Educate about how to give rescue breaths
    ▪ Make sure airway is clear
    ▪ Remove anything in the mouth
    ▪ Place one hand on chin and tilt head back to open airway
    ▪ Pinch nose closed
    ▪ Give 2 slow rescue breaths into the mouth
    ▪ Make sure chest is rising with the breaths
    ▪ Give 1 breath every 5 seconds until the person can breathe on their own
  o If person is still unresponsive after 30 seconds and naloxone is available, consider getting it at this time if you do not have to leave the person alone long enough without giving rescue breaths

• Give naloxone
  o Intramuscular administration (vial/syringe)
Remove cap of naloxone vial
- Remove cap of needle and insert needle into vial through vial rubber stopper
- Hold vial upside down
- Pull back plunger and draw up 1 mL of naloxone (0.4 mg)
  - Patients will have either a multi-dose vial (10 mL) or will draw up entire contents of single-dose vial (1mL)
- Using a needle at least 1 inch long, inject into shoulder or thigh muscle
  - May be safest and easiest to inject into the deltoid muscle

O **Intramuscular administration (auto-injector)**
- Automated voice “talks” user through injection process
- Pull off outer case; pull off red safety guard firmly
- Place black end of auto-injector against outer thigh, through clothing if needed
- A “click and hiss” sound will be heard
- Press firmly, hold in place for 5 seconds; needle retracts automatically
- Lights flash red when injection complete

O **Intranasal administration**
- Remove yellow caps from the ends of the applicator
- Remove red cap from the naloxone
- Twist the nasal adapter onto the tip of the applicator
- Twist naloxone onto the other side of the applicator
- Administer entire contents of the 2 mL syringe with approximately half (1 mL or 1 mg naloxone) administered into each nostril
  - Administering half in each nostril maximizes absorption

O After giving naloxone:
- Continue rescue breathing with 1 breath every 5 seconds if needed until emergency responders arrive
- After about 3 minutes, if patient is still unresponsive with slow or no breathing, administer another dose of naloxone

- **Stay until help arrives**
  O **Do not leave** the person alone after giving naloxone
  - It’s possible they will go back into overdose when the naloxone wears off, particularly if they took a long-acting opioid (methadone, etc)
  - Ensure they don’t take any more opioids because of withdrawal; may need help managing withdrawal symptoms
  - May need treatment for other drug overdoses

O Get medical help immediately if naloxone does not work to restore breathing and responsiveness
- Get medical help immediately if something seems wrong after giving naloxone
  - Rapid or irregular heart rate, chest pain, seizures, sudden stopping of the heart, hallucinations, loss of consciousness